

## REMARKS

Examination of claims 1-7 is reported in the present Office Action. Claims 1-7 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Claims 1-7 were rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement, and claims 5-7 were rejected under 35 U.S.C. § 112, first paragraph, because of lack of enablement. Claims 1-7 were rejected under 35 U.S.C. § 103(a) for obviousness.

### Specification Objections

In response to the objection to multiple abstracts, Applicants submit the above indicated amendment to cancel the abstract on page 11. The Examiner cited informalities in the previous amendments to the specification. Applicants submit the above amendments to pages 2 and 6 of the specification, which include correctly formatted sequence identifiers. No new matter has been added in these amendments. Applicants request that these objections be withdrawn.

### Claims Objections

Applicants have cancelled claims 1-9 and therefore request that objections to the claims be withdrawn.

### Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-7 have been rejected as being indefinite. Applicants have cancelled claims 1-7. In view of these amendments, this rejection should be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-7 have been rejected as failing to meet the written description requirement. The Examiner states that the specification “does not reasonably provide enablement for a chimeric molecule with just any signaling chains of just any cell type or without the hinge or only one CDR from the heavy and light chains of the specified antibodies or just any modified protein sequences of such.”

In response, Applicants have cancelled claims 1-7. The Examiner states that the specification is “enabling for a chimeric molecule comprising the antigen binding domain of the specific single-chain Fv molecules with the amino acid sequence of the specific antibodies with all 6 CDRs of the specific antibodies and the zeta signaling chain of the T cell receptor or other signaling domains for T cell activation and a CD8alpha hinge with or without the cysteines mutated.” In accordance with this suggestion, applicants submit new claims 10-21, which cover only chimeric molecules containing antibodies that bind PSMA and the regions set forth by the Examiner above. No new matter has been added in these amendments. In view of these amendments, Applicants request that this rejection be withdrawn.

Rejection under 35 U.S.C. § 103(a)

§ 2143 of the MPEP states:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined)

must teach or suggest all the claim limitations.

The Examiner has rejected claims 2-7 under 35 U.S.C. § 103(a) as being unpatentable over Moritz et al (Gene Therapy, 2:539-546, 1995; herein “Moritz”), in view of Fitzer-Attas et al (J. Immun., 160:145-154, 1998; herein “Fitzer-Attas”), Robinson et al. (U.S. Patent No. 5,618,920; herein Robinson), and in the case of claims 2 and 3, Murphy et al. (U.S. Patent No. 6,150,508; herein “Murphy(a)”), and in the case of claim 4, Murphy et al (J. Urology, 160:2396-2401, 1998; herein “Murphy(b)”).

These references, when considered together, do not meet the criteria set forth in the MPEP, cited above. Nowhere in these references is there a suggestion or motivation for combining the antibodies found in Murphy(a) or Murphy(b) with the chimeric molecules and hinge regions described in Moritz and Fitzer-Attas.

With regard to a reasonable expectation of success, the Examiner indicates on page 10 of the previous office action that “[p]rotein chemistry is probably one of the most unpredictable areas of biotechnology...even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein.” Moritz, in view of Fitzer-Attas, Robinson, and Murphy(a) or Murphy(b), does not provide any indication that the chimeric molecules of the invention would bind the PSMA antigen. While the prior art may teach that it would be “obvious to try” to create the functioning chimeric molecules of the invention, this is a standard has been explicitly rejected by the courts as a basis for obviousness. The Court of Appeals for the Federal Circuit has stated:

The admonition that “obvious to try” is not the standard under § 103 has been directed mainly at two kinds of error. In some cases, what would have been “obvious to try”

would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful... In others what was “obvious to try” was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it. (*In re O’Farrell*, 853 F.2d 894, \*902, paragraph 4, underline added)

In view of the “unpredictable” nature of protein biochemistry, the references do not teach that the chimeric molecules of the invention would bind PSMA antigen, activate T cells, or effectively inhibit tumor growth in vivo. Page 7 of the specification indicates that the antibodies “all have maintained antigen recognition after sFv modification.” The enclosed declaration by Dr. Junghans describes experiments showing that cells expressing the chimeric molecules of the invention became activated in the presence of the PSMA antigen, targeted cell lysis in vitro, and effectively inhibited tumor growth in an in vivo mouse model of cancer. The prediction that he chimeric molecules of the invention would function is not supported anywhere in the prior art.

Finally, Moritz, in view of Fitzer-Attas, Robinson, and Murphy(a) or Murphy(b), fail to teach all of the claim limitations. Specifically, these references do not teach a (GGSGS)<sub>3</sub> linker domain as claimed herein.

Because the above references do not meet the criteria for a prima facie case of obviousness, this rejection should be withdrawn.

The Examiner has rejected claims 2-7 under 35 U.S.C. § 103(a) as being unpatentable over Nolan et al (Clin. Cancer Res., 4:3928-3941, 1999; herein “Nolan”), in view of Fitzer-Attas, and Murphy(a) in the case of claims 2 and 3, and Murphy(b) in the case of claim 4.

These references, when considered together, do not meet the criteria set forth in the MPEP and cited above. Nowhere in these references is a suggestion or motivation for combining the antibodies found in Murphy(a) or Murphy(b) with the chimeric molecules and hinge regions described in Nolan and Fitzer-Attas.

The above indicated references do not provide a reasonable expectation of success in combining the antibodies described in Murphy(a) and Murphy(b) with the chimeric technology of Nolan and Fitzer-Attas. While the prior art may teach that it would be “obvious to try” to create the functional chimeric molecules of the invention, this is a standard, as cited above, has been explicitly rejected by the courts as a basis for obviousness. Again, there is no teaching or suggestion to combine the above references. Nor, prior to the invention, was there any the chimeric molecules of the invention would function. The enclosed declaration by Dr. Junghans describes experimental results showing that cells expressing the chimeric proteins of the invention were activated in the presence of the PSMA antigen, targeted cell lysis in vitro, and effectively inhibited tumor growth in an in vivo mouse model of cancer. Because nowhere in the prior is there support for the prediction that the chimeric molecules of the invention would function, these rejections should be withdrawn.

The Examiner has rejected claims 1 and 5-7 under 35 U.S.C. § 103(a) as being unpatentable over Moritz or Nolan in view of Fitzer-Attas, Robinson, and Cheresch et al. (Proc. Nat. Acad. Sci. USA, 82:5155-5159, 1985). Applicants note that claim 1 is cancelled, and therefore request that this rejection be withdrawn.

Double Patenting

U.S. Application No. 10/006771 has been abandoned. We therefore request that this provisional rejection be withdrawn.

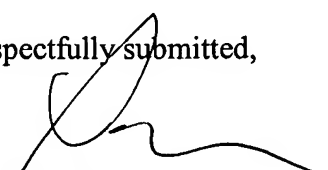
CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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